I. AMENDMENTS

In the specification:

On page 30, line 8, please delete "and" and after "(HB10794)" please add, --, 42H8 (HB 11830), 35E6 (HB 11769) and 36H3 (HB 11768).--

On page 30, please delete lines 9-10.

In the claims:

In claim 6, line 2 please replace "42H8" with --HB11830-- and please replace "35E2" with --HB11769--.

II. REMARKS

Claims 1-15 are presently pending in this application. Claims 4 and 9-14 have been withdrawn pursuant to a restriction requirement. Claims 1-3, 5-8 and 15 stand variously rejected under 35 U.S.C. §§102, 103 and 112.

Claim 6 has been amended to correct a typographical error that inadvertently references "35E6" as "35E2". Accordingly, the recitation of "35E2" has been changed to correctly recite HB11769 (i.e. 35E6). In addition "42H8" has been changed to reference its unique ATCC Accession Number, HB11830. Support for these amendment can be found throughout the specification, for example, on page 19, line 15 which indicates that antibodies produced by hybridoma 35E6 bind to a 42 kD cancer antigen and in the attached copies of the ATCC Deposit Receipts. The specification has been similarly amended to refer to the appropriate ATCC Accession Number. No new matter has been added as a result of these amendments and entry thereof is respectfully requested.

Rejections Under 35 U.S.C. § 102

Claims 1-3, 5-8 and 15 are rejected under 102(a) as allegedly anticipated by Weiner et al. (*Proc. Am. Soc. Clin. Oncol.* 13, March, 1994). Claims 1-3, 5-8 and 15 are

rejected under 102(a) as allegedly anticipated by Weiner et al. (*Proc. Am. Soc. For Cancer Res.* 35:219, March, 1994).

Applicant traverses this rejection for the reasons of record. (See, for example, Preliminary Amendment filed June 18, 1999). Nonetheless, to advance prosecution, Applicant submits herewith an affidavit stating that the non-inventor co-authors on each of the above abstracts did not conceive of the claimed subject matter. (See, MPEP 715.01(c) and *In re Katz*, 215 USPQ 14 (CCPA 1982)). Thus, Applicant has established that the art relied upon by the PTO originated with the inventor and, accordingly, the abstracts are cannot be used as references against the application. Therefore, withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C.§ 103(a)

Claims 1-3, 5-8, and 15 stand rejected as allegedly unpatentable over Hsieh-Ma et al. (Cancer Research, 1992) or Weiner et al. (Cancer Research, 1993) or Ring et al. (Breast Epithelial Antigens, 1991) in view of Fanger et al. (Critical Reviews in Immunology, 1992) or Snider et al. (J. Exp. Med. 171:1957-1963, 1990).

Applicants traverse these rejections. The pending claims specify that second binding site is capable of recognizing and binding the second antigen in an amount sufficient to induce production of antibodies in the patient. It is acknowledged by the Office that none of the primary references teach the induction of immune responses in patients. (Office Action, page 4). The secondary references, Fanger and Snider, are similarly deficient. Thus, the combinations of references cited by the Office do not render the precisely claimed invention obvious.

Nonetheless, to advance prosecution, Applicant submits herewith an affidavit establishing that the non-inventor co-authors of the Hsieh-Ma et al., Weiner et al. and Ring et al. publications are not co-inventors. (*See, e.g.*, MPEP 715.01(c)). Accordingly, the primary references, Hsieh-Ma et al., Weiner et al. and Ring et al. have been removed

as references and there is no longer basis for the Examiner's rejections. Therefore, withdrawal of these rejections is respectfully requested.

Rejections Under 35 U.S.C. § 112, First Paragraph

Claim 6 stands rejected under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to use the claimed invention. In particular, it is alleged that (1) the specification as filed does not provide support for bispecific antibodies wherein the second antigen binding portion recognizes antigens which bind to antibody 35E2, HB 10789 or HB10793; and (2) the Deposit Requirements of 37 CFR 1.801-1.809 have not been satisfied with respect to 35E2, HB10789 and HB10793. Applicants address each issue in turn.

Antibodies Produced by 35E6, HB10789 and HB10793

The Office Action states that claim 6, as amended in the preliminary amendment filed June 18, 1999, recites limitations which introduce new concepts and that the specification does not have support for bispecific antibodies where the second antigen binding portion is recognized by antibodies produced by 35E2, HB 10789 or HB10793. (Office Action, page 5).

Applicants traverse the rejection and supporting remarks.

To advance prosecution, claim 6 was amended in the preliminary amendment to define the cancer antigen in relation to antibodies that recognize the antigen rather than by the molecular weight of the antigen. Inadvertently, the preliminary amendment contained a typographical error which improperly referenced hybridoma 35E2 rather than 35E6. This typographical error has been corrected herein by amending claim 6 to recite the ATCC Accession Number of hybridoma 35E6. A copy of the appropriate ATCC Deposit Receipt is attached hereto. Further, the specification, as filed, clearly indicates

that antibodies produced by 35E6 recognize a 42 kD cancer antigen (page 19, line 15), as originally recited in claim 6. In addition, the specification teaches that the second binding site of the bispecific antibody may be derived from a monoclonal antibody produced by 35E6 (page 6, line 6). Accordingly, amending claim 6 to recite 35E6 (*i.e.* HB11769) does not introduce new concepts into the claims.

Similarly, the recitation of HB 10789 (106A10) and HB 10793 (421E8) in claim 6 does not introduce new concepts into the claims. Original claim 6 recited that suitable cancer antigens included a 55 kD antigen, for example HB 10789 (page 19, line 16). For its part, HB 10793 recognizes "cancer antigens from cancer including colon cancer and other cancers as well" (page 19, lines 19-20). Furthermore, the specification teaches that HB 10789 and HB 10793 are useful in producing antibodies that can be used to derive a second binding site of a bispecific antibody. (See, page 6, line 6 (HB10789) and page 6, line 10 (HB 10793)). Thus, Applicant recognized, at the time of filing, that these antibodies were useful in the methods of claim 6.

In sum, at the time of filing, Applicants were in possession of methods involving bispecific antibodies where the second binding site recognized and bound to a cancer antigen recognized by antibodies produced by 35E6, HB10789 and HB10793. (See, Summary of Invention, page 6). Therefore, no new concepts have been introduced by rewording claim 6 to refer to hybridomas which produce the second antibody, rather than to the antigen recognized by the second antibody. There is ample support for the recitation of 35E6, HB 10789 or HB10793 in claim 6 and Applicant respectfully requests that this rejection be withdrawn.

Deposit of Hybridomas

Claim 6 is also rejected under Section 112, first paragraph because the public availability of hybridomas 35E6, HB 10789 and HB 10793 is allegedly not ensured.

Applicant traverses this rejection in part and believe it is overcome for the reasons outlined below. Applicant directs the Examiner's attention to page 30, lines 3 and 8 of the specification which indicate, respectively, that hybridomas having ATCC Accession Numbers HB 10789 and HB10793, were deposited under the provisions of the Budapest Treaty and that the viability and public availability have been assured by the assignee, Chiron Corporation.

With regard to 35E6, this hybridoma was deposited with the ATCC on December 6, 1994 and given Accession No. HB11769. Hybridoma 42H8 was deposited on February 7, 1995 and given Accession No. HB11830. In addition, Applicant's representative has requested assurance of public availability in compliance with the Budapest Treaty in the form of a declaration from the Assignee of the present application. The declaration will be forwarded to the Examiner as soon as it is received.

In view of the above arguments and amendments, the Applicant submits that claim 6 is enabled and that the rejection of this claims under 35 U.S.C 112, first paragraph, should be withdrawn upon receipt of the declaration from the Assignee.

III. CONCLUSION

In view of the foregoing, Applicant submits that the claims are now in condition for allowance and requests early notification to that effect.

Please direct all further communications regarding this application to:

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Respectfully submitted,

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